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ABSTRACT

The physical and neurobehavioral findings at 3 years of age for 39 children born to mothers on methadone- maintenance and 23 children born to drug-free comparison mothers are reported. The methadone children had a higher incidence of head circumferences less than the third percentile, nystagmus/strabismus, and otitis media. No differences were found in number of emergency room visits, infections, or hospitalizations. Mean scores on the Merrill-Palmer Scale of Mental Tests were not significantly different, but more methadone children had scores less than the 25th percentile. Spontaneous language production was low in both groups of children. The neurological evaluation and head circumference correlated with the Merrill-Palmer scores. It is concluded that methadone affected some children more adversely than others, but it is important to examine how psychosocial and environmental factors interact with methadone maintenance in shaping development. Includes 11 references. (JDD)

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Children of methadone-maintained mothers: Three-year follow-up

Condensed title: Children of methadone mothers at age three

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ABSTRACT

For the past three years we have followed a group of children born to mothers on methadone-maintenance and to drug-free comparison mothers. This report describes our physical and neurobehavioral findings at three years of age for 39 methadone and 23 drug-free children. The methadone children still had a higher incidence of: head circumferences less than 3 percentile, nystagmus/strabismus, and otitis media. Although the mean Merrill-Palmer scores were not significantly different, significantly more methadone children had scores less than the 25 percentile. Spontaneous language production was low in both groups of children. The neurological evaluation and head circumference correlated with the Merrill-Palmer scores. In this study, methadone affected some children more adversely than others. It is important to examine how psychosocial and environmental factors interact with methadone maintenance in shaping development.

Methadone maintenance has been the treatment of choice for heroin addiction for the past several years. The effects of methadone maintenance during pregnancy on the newborn and young child have been described in several reports (1-6). Neonatal withdrawal occurs in 70-90% of newborns, lasting from a few weeks to several months (1-3). As far as long term follow-up during childhood is concerned, some investigators have described mild neurobehavioral deficits while others have found none (4, 6, 7, 8).

Since 1977 we have followed longitudinally from birth the physical and neurobehavioral development of a group of children born to methadone-maintained mothers and to matched drug-free mothers. This report describes our findings at 3 years of age. Our 18 and 24 months data for these children have been described previously (9, 10).

Methods

Subjects:

Fifty-seven methadone-maintained mothers were followed through pregnancy and birth; 62 of their children (three sibling pairs) were enrolled in the follow-up. Thirty-one comparison mothers and 32 of their newborns (one sibling pair) were enrolled following birth, and were matched for socioeconomic class, sex, gestational age and birthweight $\pm$ 250 gms. At 36 months of age 39 methadone-maintained mothers and their children and 23 drug-free mothers and their children remained in the study. Our loss rate was approximately 36% in the experimental group and approximately 28% in the drug-free group. A comparison of the

continuing versus lost subjects revealed no differences in maternal and neonatal characteristics.

Table I is a summary of the maternal characteristics of the continuing subjects. The mean ages of the mothers are significantly different but both are well within the normal age range for child bearing. The incidence of obstetrical complications (i.e. pre-eclampsia, amnionitis, ROM and premature labor) is higher in the methadone-maintained mothers. Sixty-two percent of the methadone-maintained mothers were multidrug abusers, (i.e. Elavil, barbiturates, diazepam) and 86% (vs. 25% in the comparison group) were cigarette smokers. The mean methadone dose was 41 +/- 3 mg/day with mean months on methadone maintenance 35 +/- 4.

Table II is a summary of the neonatal characteristics of the continuing subjects. There were 19 male and 20 female children in the methadone group and 13 male and 10 female children in the drug-free group. There were no differences in birthweights, gestational ages or Apgar scores.

Procedure:

Each study infant was evaluated physically and neurologically in the nursery and then was seen in the follow-up clinic every 2 months for the first year and every 3 - 6 months during the second and third years. Each visit consisted of physical and neurobehavioral evaluations. We also provided well-baby and emergency care as well as social service assistance. More complete details have been previously published (9, 10).

At 3 years of age these children received a thorough physical examination, and neurological and developmental evaluations. In addition, the number and type of infections, clinic/emergency room visits and referrals were recorded.

As part of the 36 months behavioral evaluation, the children were given the Merrill-Palmer Scale of Mental Tests. In addition, a sample of spontaneous language production was obtained in a free play situation. Mother and child were seated in a playroom area and given a set of wooden puzzles of varied difficulty to do, followed by a box of toys to play with. This play session lasted 30 minutes and was videotaped. In the hope of eliciting expanded utterances, the observer encouraged verbalization from the child. A full transcription of each language-play session was prepared and the mean length of utterance (MLU) for each child was computed according to the procedures outlined by Brown (11). The MLU is based on 50 rather than 100 utterances because the play session was only 30 minutes long.

Social service evaluations were also done at 3 years of age regarding primary caretakers, income status, employment and problem presentation.

Statistical Analysis

Significance of group differences was analyzed with t-tests. Chi square and the Fischer's Exact test were used to analyze frequency distributions.

Results

There was no difference in the number of years of maternal education by child's age 36 months. However, more of the drug-free than methadone mothers were working and off welfare ($p < .02$). Further, the methadone-maintained mothers presented many more emotional and social problems than the drug-free group ($p < .07$). Ten percent of the mothers in the experimental group detoxed from methadone during this period. By three years of age, 23% of the children of methadone-maintained mothers versus 4% of the children of drug-free mothers lived with grandmothers, foster or adoptive parents.

In Table III, which summarizes growth parameters at 3 years of age, the only significant finding was a higher incidence of head circumferences less than the 3 percentile in the methadone group ($p < .03$). The head circumferences did not correlate with either weight or height. With regard to the rate of infections, the methadone children still had a higher incidence of otitis media during the second year of life as reported previously ($p < .03$).

No differences were found between the two groups in number of emergency room visits or number of infections or hospitalizations. However, the methadone children continued to show a higher incidence of strabismus and/or nystagmus ($p < .001$). These children are all being followed by the ophthalmology clinic. No other anomalies were noted. The neurological evaluations at age three years (i.e. tone, coordination, reflexes and developmental milestones) showed a higher incidence of

abnormalities in tone and coordination in the methadone group ($p < .07$) (Table III).

The mean Merrill-Palmer scores were not significantly different; however, scores lower than the 25 percentile were significantly more frequent ($p < .003$) in the methadone group, as illustrated in Table III. The analysis of spontaneous language production with mean length of utterance (MLU) was based on 50 rather than on 100 utterances. However, even with this lower utterance requirement, it was necessary to exclude 5 methadone and 6 comparison children from the analysis because their half-hour language sample included less than 50 utterances. For the methadone subjects, the mean MLU was $2.71 \pm .66$ and for the comparison subjects, it was $3.14 \pm .66$ ($p < .07$). These MLU samples are clearly lower than those reported for middle class samples (11).

Correlations between prenatal, neonatal, neurological and developmental indices were analyzed. For purposes of analysis a score of zero was assigned to each comparison subject for the variables associated with drug abuse (number of months on methadone, methadone dose, multidrug abuse, severity of withdrawal). Obstetrical complications correlated with methadone dose, number of months on methadone maintenance and the severity of neonatal narcotic abstinence syndrome. Multidrug abuse correlated with birthweight and 5 minute Apgar score. The maternal methadone dose correlated with birthweight and head size at birth. At 36 months of age, the neurological evaluation and

head circumferences correlated with the Merrill-Palmer scores and percentiles. In addition, the 36 months neurological evaluation correlated with gestational age, birthweight and severity of withdrawal.

Discussion

In our study, at three years of age the children of methadone-maintained mothers did not differ from the drug-free comparison children in somatic growth except for a higher incidence of small head sizes. This has also been described by Wilson et al. (4). On neurological evaluations, the methadone children showed a higher incidence of soft signs. There were no group differences in mean scores on the Merrill-Palmer Scales, again corroborating the findings of other methadone follow-up studies (4, 6, 8). However, the measures of central tendency used to compare group means can mask group differences in score distribution, and this is, in fact, what happened here. For closer examination of the data revealed that there were more extreme scores in the methadone group, and much less variance in the comparison group. In addition, in the methadone group there was a consistent pattern of correlations between head size, neurological evaluation at each time point, and developmental scores (the Bayley Scales at 18 and 24 months and the Merrill-Palmer Scale at 36 months).

These findings indicate that simply analyzing overall group scores does not provide an adequate comparison of group

performance. A more detailed and qualitative analysis of patterns of performance within each group is necessary.

Summary

In evaluating the developmental effects of maternal methadone maintenance during pregnancy, it is evident that some children are more adversely affected than others. The absence of a clear relation between the drug history variables (length of maternal methadone maintenance, size of methadone dose, severity of neonatal narcotic abstinence syndrome) and developmental measures suggests that the psychosocial and environmental factors encompassed by maternal methadone maintenance must be considered as well. For the child born to methadone-maintained mothers has not simply been exposed to a drug in utero; he must also contend with the increased emotional and family instability and environmental chaos that is characteristic of the drug culture. Thus, the effect of maternal methadone maintenance on the child's development reflects the particular interaction between perinatal and environmental factors in the life of each child.

TABLE 1
SUMMARY OF MATERNAL CHARACTERISTICS

<u>Characteristic</u>	<u>Methadone (n=39)</u>	<u>Drug-free (n=23)</u>
Age*	27.10 $\pm$.58	23.74 $\pm$ 1.14
Gravida*	3.18 $\pm$.28	2.30 $\pm$ 1.14
Para*	1.28 $\pm$.19	1.00 $\pm$.23
Abortions*	.92 $\pm$.20	.30 $\pm$.10
<u>Race (%)</u> : Black	75	83
Hispanic	10	13
White	15	4
Positive Obst. Hx. (%)	33	9
<u>Drug Abuse Hx. (%)</u> :		
Multidrug	62	0
Alcohol	15	0
Smoking (> 1 pack/day) %	86	25
Methadone does (mg/day)*	41.20 $\pm$ 3.1	—
<u>Social Hx.:</u>		
Education (years)	9 - 14	9 - 16
Welfare (%): At birth	89	65
At 3 years	85	52
Job at 3 years (%)	13	35
* M $\pm$ SE		

TABLE 11
INFANT CHARACTERISTICS

<u>Characteristic</u>	<u>Methadone</u>	<u>Drug-free</u>
Birthweight (gms)*	2814.3 $\pm$ 86.7	3073.9 $\pm$ 112.8
Gestational age (weeks)*	38.6 $\pm$.3	39.0 $\pm$.5
Premature (%)	13 (33 weeks)	9 (30 weeks)
SGA (%)	13 (<10%)	0
Apgar Score: *		
1 minute	7.7 $\pm$.3	7.7 $\pm$.3
5 minutes	8.7 $\pm$.1	8.9 $\pm$.0
Sex (n):		
Males	19	13
Females	20	10
Severity of withdrawal (%):		
Severe	21 (all treated)	—
Moderate	49	—
Mild	30	—

* M $\pm$ SE

TABLE III
SUMMARY OF CHILDREN'S CHARACTERISTICS AT 3 YEARS OF AGE

<u>Variable</u>	<u>Methadone</u>	<u>Drug-free</u>
MEDICAL		
Head circumference <3%ile (%)	34	13**
Weight <10%ile (%)	26	9
Height <10%ile (%)	23	17
Rate of infection:		
Otitis media < 2/year (%)	21	4**
NEUROBEHAVIORAL		
Neurological evaluation:		
Suspect → abnormal (%)	13	32**
Merrill-Palmer Scale (M ± SE)		
MPS	44.6 ± 2.05	46.3 ± 2.3
MP%	51.3 ± 4.26	58.3 ± 4.5
< 25%ile (%)	24	4***
> 75%ile (%)	24	17

*approaches
significance,
p<.07

**p<.05

***p<.01

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